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Brief Clinical Report

Smith-Lemli-Opitz Syndrome Diagnosed in a 130-Year-Old Anatomical Specimen

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The *Museum Vrolik* collection of human anatomy comprises 360 recently redescribed specimens with congenital anomalies. The external findings in one of these specimens, originally described by Willem Vrolik (1801–1863) 130 years ago, were suggestive of Smith-Lemli-Opitz (SLO) syndrome. Cholesterol synthesis was analyzed in skin biopsies, obtained from the suspected SLO specimen and a control specimen. The cholesterol levels in the SLO specimen and in the control specimen were in the proportion of 1 to 45. This confirms the diagnosis in this specimen which, to our knowledge, represents the oldest known case of SLO syndrome. Am. J. Med. Genet. 68:257–259, 1997. © 1997 Wiley-Liss, Inc.

KEY WORDS: anatomical specimen; cholesterol synthesis; dermatoglyphics; early report; Smith-Lemli-Opitz syndrome; Willem Vrolik

INTRODUCTION

The Department of Anatomy and Embryology of the University of Amsterdam in the Netherlands has a large collection of anatomical and pathological specimens. It was begun by the Dutch anatomists Gerardus Vrolik (1775–1859) and his son Willem Vrolik (1801–1863), and was gradually enlarged since then. At present it comprises over 5,000 specimens, mainly of human anatomy, embryology, and pathology. Recently we recatalogued and redescribed 360 specimens with congenital anomalies, according to contemporary morphological points of view [Oostra et al., 1994, submitted for publication].

Here we describe a specimen, part of the original

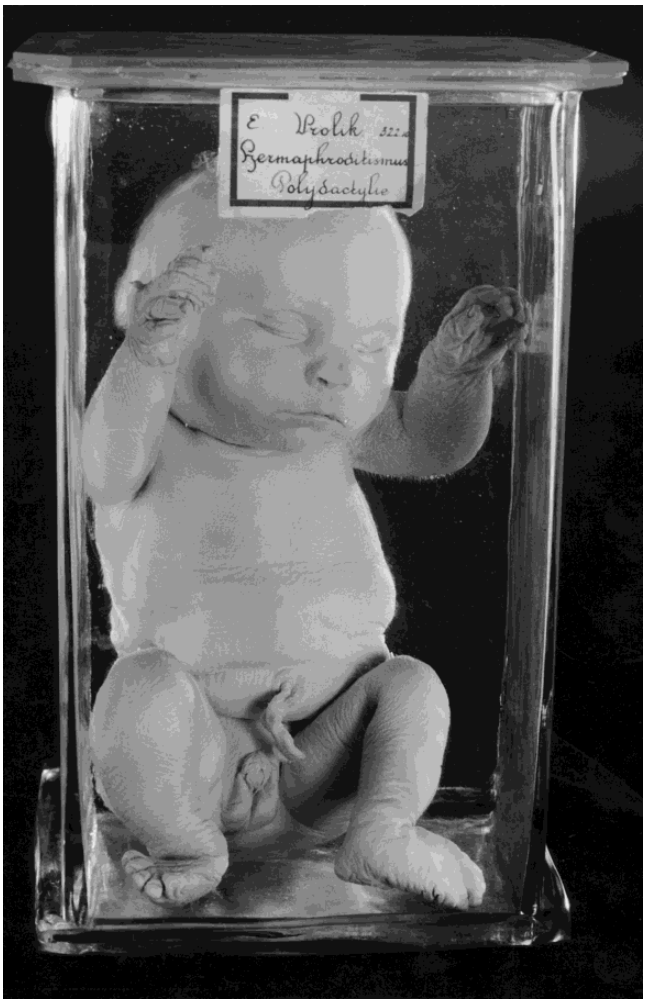

Fig. 1. Frontal view of fetus, showing short stature, mild microcephaly, round face, epicanthic folds, broad nasal bridge, and small nose.

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Fig. 2. Lateral view, showing relatively high nasal bridge, long philtrum, mild micrognathia, and postaxial hexadactyly of the hands.

Vrolik collection, with external findings suggestive of Smith-Lemli-Opitz (SLO) syndrome, in which we tried to verify the diagnosis.

CLINICAL REPORT

The specimen is a newborn infant from Willem Vrolik's collection of congenital anomalies. It was originally fixed in 70% ethanol and refixed in 4% formaldehyde solution in later years. It was described in a catalogue of the collection which was initiated by Willem Vrolik and completed after his death by J.L. Dusseau in 1865 [Dusseau, 1865]. According to this catalogue the fetus had hypospadias, duplication of the little finger of both hands, and a connection between a few toes of both feet. It was not described in Willem Vrolik's famous illustrated handbook "Tabulae ad Illustrandam Embryogenesin Hominis et Mammalium Tam Naturalem Quam Abnormem," issued between 1844–1849 [Vrolik, 1849], nor was it found in any of his earlier works, nor in any of his father's. Therefore, we assume that it was obtained after 1849 and probably before his death in 1861, but in any case before 1865. Thus, this fetus is at least 130 years old.

On examination (Figs. 1–4) there was short stature (CRL 27 cm), mild microcephaly (OFC 31.5 cm), a round face, broad nasal bridge, epicanthal folds, small nose, long philtrum, mild micrognathia, short neck, and symmetrical postaxial hexadactyly of the hands. There was incomplete syndactyly of the second and third toes of both feet, leaving the distal phalanges free. The feet, especially the right one, showed a valgus deformity. There was genital ambiguity, with an undif-

Fig. 3. Frontal view of lower part of the body, showing ambiguous genitalia and valgus deformity of the feet.

Fig. 4. Detail of left foot, showing typical "fork-shaped" syndactyly of the second and third toes.

ferentiated genital tubercle, a slit-like urethral orifice, and a deep scrotal fold. Based on these findings, the diagnosis of SLO syndrome was made.

Additional investigations were performed to verify the diagnosis. MRIs of the head and of the thoracic, abdominal, and pelvic regions were made in three directions; these showed remarkably few internal defects. There were no evident cerebral abnormalities, except for a dubious pachygyria, which is more likely an artifact caused by decomposition or prolonged fixation. Cerebellar hypoplasia was not found. There was a large median cleft of the palate. No signs of abnormal pulmonary lobation were found. Abnormalities in cardiac septation could not be sufficiently assessed. The liver, gallbladder, spleen, kidneys, and adrenal glands were all normal in shape and structure.

Dermatoglyphic analysis was hampered by the prolonged fixation of the specimen in ethanol and formaldehyde, and the severely wrinkled skin of the fingertips, which made it impossible to take fingerprints using conventional methods. Therefore, we stained the fingertips with ink and studied them directly, using a 256× enlarging surgical microscope (Zeiss Opton). Thus, we identified an arch on the left thumb, whorls on the first and sixth fingers of the right hand, and ulnar loops on the left third finger and on the right fourth and fifth fingers. Unfortunately, the patterns on the other digits were not identifiable.

Skin biopsies were taken to establish the expected male genotype with fluorescence in situ hybridization (FISH). Results are presently inconclusive.

Impairment of cholesterol synthesis was studied using as a control sample a skin biopsy of another specimen with a perioral teratoma, which had been fixed in the same way. The biochemical procedure was a variant of that described by Tint et al. [1994], and will be published separately (Schutgens et al., in preparation). Two biopsies were taken from the SLO specimen and the control specimen, which were investigated separately. The first biopsy of the SLO specimen contained 0.6 μg cholesterol/g moist weight skin; the control specimen contained 27 μg cholesterol/g moist weight skin (ratio 1:45). The second biopsy of the SLO specimen contained 2.9 μg cholesterol/g dry skin, the control specimen 135 μg cholesterol/g dry skin (ratio 1:46.6) 7-dehydro- and 8-dehydroxycholesterol were not detected in either specimen using mass spectometry, as was anticipated because of the degradation of 7-dehydrocholesterol in light.

DISCUSSION

To the best of our knowledge, Willem Vrolik's specimen represents the oldest known case of SLO syndrome. His description of the specimen in the original museum catalog appeared 100 years before the classical delineation of the syndrome by Smith et al. [1964]. Many other specimens of well-known entities can be found in the Vrolik collection [Oostra et al., 1994, 1997a,b].

Museum collections of anatomical and pathological specimens are rich sources for studying human dysmorphology, and certainly are a joy to the "true" dysmorphologist's heart.

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